

In the Claims

Please replace all prior versions, and listings, of claims in the application with the following list of claims:

1. (Currently amended) ~~An anti-Epidermal Growth Factor Receptor (EGFR) polypeptide comprising at least one~~ A single domain antibody directed against EGFR, wherein said single domain antibody inhibits and/or blocks the interaction between EGF and EGFR.
- 2-45. (Canceled)
46. (New) A single domain antibody directed against Epidermal Growth Factor Receptor (EGFR), wherein said single domain antibody is selected from the group consisting of
 - a sequence represented by SEQ ID NO: 6,
 - a sequence with a homology of more than 70% with SEQ ID NO: 6,
 - a functional portion of SEQ ID NO: 6 wherein the functional portion is capable of binding its target with an affinity of at least 1×10^{-6} M; and,
 - a functional portion of SEQ ID NO: 6 wherein the functional portion comprises a partial deletion of the complete amino acid sequence and still maintains the binding site(s) and protein domain(s) necessary for the binding of and interaction with EGFR.
47. (New) The single domain antibody according to claim 46, wherein the single domain antibody corresponds to a sequence with a homology of more than 80% with SEQ ID NO: 6.
48. (New) The single domain antibody according to claim 46, wherein the single domain antibody corresponds to a sequence with a homology of more than 90% with SEQ ID NO: 6.
49. (New) The single domain antibody according to claim 46, wherein one or more of the Camelidae amino acids of the single domain antibody are replaced by counterpart amino acids of the human consensus sequence.

50. (New) The single domain antibody according to claim 49 comprising one or more of the following mutations: FR1 positions 1, 5, 28 and 30; the hallmark amino acid at position 44 and 45 in FR2; FR3 residues 74, 75, 76, 83, 84, 93 and 94; and positions 103, 104, 108 and 111 in FR4; wherein the numbering is according to the Kabat numbering.

51. (New) The single domain antibody according to claim 49 wherein the hydrophilic residues at positions 44 and 45 are replaced by their counterpart human hydrophobic residues; wherein the numbering is according to the Kabat numbering.

52. (New) The single domain antibody according to claim 46, wherein the single domain antibody competes for, or inhibits, binding of a natural ligand to EGFR.

53. (New) The single domain antibody according to claim 52, wherein said natural ligand is Epidermal Growth Factor (EGF).

54. (New) The single domain antibody according to claim 46, wherein the single domain antibody is capable of binding to its target with an affinity of at least 1×10^{-6} M.

55. (New) An anti-Epidermal Growth Factor Receptor (EGFR) polypeptide consisting essentially of the single domain antibody according to claim 46 and at least one single domain antibody directed against one or more serum proteins.

56. (New) The anti-EGFR polypeptide according to claim 55, wherein said serum protein is selected from the group consisting of serum albumin, serum immunoglobulins, thyroxine-binding protein, transferrin, and fibrinogen or a fragment thereof.

57. (New) The anti-EGFR polypeptide according to claim 55, wherein said anti-EGFR polypeptide is selected from the group consisting of
a sequence represented by SEQ ID NO: 33,

a sequence with a homology of more than 70% with SEQ ID NO: 33;
a functional portion of SEQ ID NO: 33, wherein the functional portion is capable of binding its target with an affinity of at least 1×10^{-6} M; and,
a functional portion of SEQ ID NO: 33 wherein the functional portion comprises a partial deletion of the complete amino acid sequence and still maintains the binding site(s) and protein domain(s) necessary for the binding of and interaction with EGFR, and
a humanized sequence of SEQ ID NO: 33 wherein one or more of the Camelidae amino acids of the anti-EGFR polypeptide are replaced by counterpart amino acids of the human consensus sequence.

58. (New) The anti-EGFR polypeptide according to claim 55, wherein said anti-EGFR polypeptide corresponds to a sequence with a homology of more than 80% with SEQ ID NO: 33.

59. (New) The anti-EGFR polypeptide according to claim 55, wherein said anti-EGFR polypeptide corresponds to a sequence with a homology of more than 90% with SEQ ID NO: 33.

60. (New) An anti-Epidermal Growth Factor Receptor (EGFR) polypeptide consisting essentially of the single domain antibody according to claim 46 and at least one single domain antibody selected from the group consisting of anti-IFN-gamma single domain antibody, anti-TNF-alpha single domain antibody, anti-TNF-alpha receptor single domain antibody and anti-IFN-gamma receptor single domain antibody.

61. (New) An anti-Epidermal Growth Factor Receptor (EGFR) polypeptide consisting essentially of two or more single domain antibodies according to claim 46.

62. (New) The anti-EGFR polypeptide according to claim 61, wherein the two or more single domain antibodies are different in sequence.

63. (New) The anti-EGFR polypeptide according to claim 61, wherein the two or more single domain antibodies are identical in sequence.
64. (New) The anti-EGFR polypeptide according to claim 61, wherein the two or more single domain antibodies are fused genetically at the DNA level.
65. (New) The anti-EGFR polypeptide according to claim 61, wherein the two or more single domain antibodies are linked to each other directly.
66. (New) The anti-EGFR polypeptide according to claim 61, wherein the anti-EGFR polypeptide is a trivalent or tetravalent molecule.
67. (New) A composition comprising the single domain antibody according to claim 46 and a suitable pharmaceutical vehicle.
68. (New) A composition comprising the anti-EGFR polypeptide according to claim 55 and a suitable pharmaceutical vehicle.
69. (New) A composition comprising the anti-EGFR polypeptide according to claim 60 and a suitable pharmaceutical vehicle.
70. (New) A composition comprising the anti-EGFR polypeptide according to claim 61 and a suitable pharmaceutical vehicle.
71. (New) The composition according to claim 67, wherein the composition is formulated for administration orally, vaginally, rectally, parenterally, intra-nasally, by inhalation, sublingually, intravenous, intramuscular, topical or by subcutaneous routes.

72. (New) The composition according to claim 68, wherein the composition is formulated for administration orally, vaginally, rectally, parenterally, intra-nasally, by inhalation, sublingually, intravenously, intramuscularly, topically or by subcutaneous routes.

73. (New) The composition according to claim 69, wherein the composition is formulated for administration orally, vaginally, rectally, parenterally, intra-nasally, by inhalation, sublingually, intravenously, intramuscularly, topically or by subcutaneous routes.

74. (New) The composition according to claim 70, wherein the composition is formulated for administration orally, vaginally, rectally, parenterally, intra-nasally, by inhalation, sublingually, intravenously, intramuscularly, topically or by subcutaneous routes.

75. (New) The composition according to claim 67, wherein the composition is formulated for injection or infusion.

76. (New) The composition according to claim 68, wherein the composition is formulated for injection or infusion.

77. (New) The composition according to claim 69, wherein the composition is formulated for injection or infusion.

78. (New) The composition according to claim 70, wherein the composition is formulated for injection or infusion.

79. (New) A pharmaceutical composition for blocking of ligand binding to Epidermal Growth Factor Receptor (EGFR) comprising the single domain antibody of claim 46 and a carrier.

80. (New) A pharmaceutical composition for blocking of ligand binding to Epidermal Growth Factor Receptor (EGFR) comprising the anti-EGFR polypeptide of claim 55 and a carrier.

81. (New) A pharmaceutical composition for blocking of ligand binding to Epidermal Growth Factor Receptor (EGFR) comprising the anti-EGFR polypeptide of claim 60 and a carrier.
82. (New) A pharmaceutical composition for blocking of ligand binding to Epidermal Growth Factor Receptor (EGFR) comprising the anti-EGFR polypeptide of claim 61 and a carrier.
83. (New) A method for inhibiting the interaction between Epidermal Growth Factor (EGF) and Epidermal Growth Factor Receptor (EGFR) comprising administering the single domain antibody of claim 46.
84. (New) A method for inhibiting the interaction between Epidermal Growth Factor (EGF) and Epidermal Growth Factor Receptor (EGFR) comprising administering the anti-EGFR polypeptide of claim 55.
85. (New) A method for inhibiting the interaction between Epidermal Growth Factor (EGF) and Epidermal Growth Factor Receptor (EGFR) comprising administering the anti-EGFR polypeptide of claim 60.
86. (New) A method for inhibiting the interaction between Epidermal Growth Factor (EGF) and Epidermal Growth Factor Receptor (EGFR) comprising administering the anti-EGFR polypeptide of claim 61.
87. (New) A kit for screening agents that modulate Epidermal Growth Factor Receptor (EGFR)-mediated disorders comprising the single domain antibody of claim 46.
88. (New) A kit for screening agents that modulate Epidermal Growth Factor Receptor (EGFR)-mediated disorders comprising the anti-EGFR polypeptide of claim 55.

89. (New) A kit for screening agents that modulate Epidermal Growth Factor Receptor (EGFR)-mediated disorders comprising the anti-EGFR polypeptide of claim 60.
90. (New) A kit for screening agents that modulate Epidermal Growth Factor Receptor (EGFR)-mediated disorders comprising the anti-EGFR polypeptide of claim 61.
91. (New) A kit for screening for a disorder characterized by dysfunction of Epidermal Growth Factor Receptor (EGFR) comprising the single domain antibody of claim 46.
92. (New) A kit for screening for a disorder characterized by dysfunction of Epidermal Growth Factor Receptor (EGFR) comprising the anti-EGFR polypeptide of claim 55.
93. (New) A kit for screening for a disorder characterized by dysfunction of Epidermal Growth Factor Receptor (EGFR) comprising the anti-EGFR polypeptide of claim 60.
94. (New) A kit for screening for a disorder characterized by dysfunction of Epidermal Growth Factor Receptor (EGFR) comprising the anti-EGFR polypeptide of claim 61.